グリオキサルのラット及びマウスを用いた経口投与によるがん原性予備試験(混水試験)報告書

試験番号

2週間試験:ラット/0222;マウス/0223

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 MOUSE : MALE
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 MOUSE: FEMALE
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 (TWO-WEEK STUDY: SUMMARY)
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 RAT : FEMALE : SACRIFICED ANIMALS
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 MOUSE: MALE: SACRIFICED ANIMALS
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 (TWO-WEEK STUDY: SUMMARY)
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APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0222 ANIMAL : RAT F344

REPORT TYPE : A1 2

SEX : MALE

PAGE: 1

Clinical sign	Group Name	∧dmini:	stration W	ek-day											
		1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	
AT A THE	0	•	•	•	•	•		٥	0	0	0	0	0	0	0
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	•	0	v	•	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	U
	9000ppm	0	0	0	0	0	0	0	0	0	1	1	i	1	1
ORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	4	4	4	4
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	3	3	0	0	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	. 0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	2	5	5	2	2	3
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	mqq0008	0	0	0	0	0	0	0	7	7	7	6	4	4	5

(HAN190)

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0222 ANIMAL: RAT F344 REPORT TYPE : A1 2

PAGE: 2 SEX : MALE

Clinical sign	Group Name	Adminis	stration We	ek-day											
		1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	l .	1	1
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	maa0000	0	0	0	0	0	0	0	0	0	1	2	1	1	1
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	mqq0003	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	1	2	1	1	1
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	1	1	1	1	1	1	1	0
	9000pm	0	0	0	0	9	9	9	9	9	8	7	4	4	4
DLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	0
	9000pm	0	0	0	0	4	4	4	4	4	8	7	5	5	4
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	Ô	Õ	0	0	0	0	0	0	1	3	1	1	1

(IIAN190)

APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX: FEMALE

PAGE: 3

linical sign	Group Name	Admini	stration We	eek-day											
		1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	9000ppm	0	0	0	0	0	0	0	1	2	2	2	2	4	5
DRIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000pm	0	0	0	0	0	0	1	1	2	2	4	4	4	4
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	0	0	1	1	0
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	Ö	0	1	1	2	2	1	1
	9000ppm	0	0	0	0	0	2	3	1	5	6	6	4	2	1
OILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	Ö	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	Ō	Ö	0	Ö	Ö	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	Ö	0	0	0	Ô	0	0	0	0	Ô	0
	9000ppm	Ö	0	0	Ő	0	0	0	0	1	1	1	0	1	0

STUDY NO.: 0222 ANIMAL: RAT F344 REPORT TYPE: A1 2 CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE: 4

	1-1 1	1-2 1	1-3	1-4	1-5	1-6	1 7	0.1	0.0	2-3	2-4	2-5	2-6	0.7
	1	1	•		1 0	1-0	1-7	2-1	2-2	2-3	2-4	4-0	4-0	2-7
			1	1	1	1	1	1	1	1	1	1	1	1
													·	
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6000ppm	0	0	0	0	0	0	0	1	2	3	3	3	2	3
9000pm	0	0	0	0	0	2	2	6	7	6	6	4	2	1
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4000ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	0	0	0	0	1	1	2	2	2	4	4	4	2	5
9000pm	0	0	0	0	3	3	6	5	4	5	6	4	2	1
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	Q	0	0	0	0	0	0	0	0	Ö	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	1	0	0
9000pm	0	0	0	0	0	0	1	0	1	1	3	2	1	0
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0		0	0	0	0	0	0	0	0	0	0
	0	0	0		0	0	0	0	0	0	0	0	0	0
	0	0	0		0	0	0	0	0	0	0	1	0	0
9000pm	0	0	0	0	0	0	1	0	1	1	3	2	1	0
Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	-	-	-	0	0	0	0	0	Õ	Ô
	0	Ö	o 0	0	-	0	0	•	•	0	0	0	0	0
	0	0	-				-			2.	2	2		ĭ
	ő	•		-										1
	2667ppm 4000ppm 6000ppm 9000ppm 9000ppm Control 1778ppm 4000ppm 9000ppm 9000ppm 4000ppm 2667ppm 4000ppm 9000ppm 6000ppm 9000ppm Control 1778ppm 2667ppm 4000ppm 9000ppm	2667ppm 0 4000ppm 0 6000ppm 0 9000ppm 0 9000ppm 0 1778ppm 0 2667ppm 0 4000ppm 0 6000ppm 0 9000ppm 0 1778ppm 0 2667ppm 0 2667ppm 0 2667ppm 0 2667ppm 0 2667ppm 0 0 Control 0 1778ppm 0 2667ppm 0 6000ppm 0 9000ppm 0 Control 0 1778ppm 0 2667ppm 0 Control 0 1778ppm 0 2667ppm 0 6000ppm 0 Control 0	2667ppm 0 0 0 4000ppm 0 0 0 6000ppm 0 0 0 9000ppm 0 0 0 Control 0 0 2667ppm 0 0 0 4000ppm 0 0 0 Control 0 0 0 4000ppm 0 0 0 Control 0 0 0 1778ppm 0 0 0 1778ppm 0 0 0 2667ppm 0 0 0 2667ppm 0 0 0 Control 0 0 0 1778ppm 0 0 0 2667ppm 0 0 0 Control 0 0 0 1778ppm 0 0 0 Control 0 0 0 0 0 Control 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ррт 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667cpm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667ppm	2867 ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2667-ppm 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

STUDY NO.: 0222 ANIMAL: RAT F344 REPORT TYPE: A1 2 CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE: 5

Clinical sign	Group Name	Admini:	stration W	eek-day											
		1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	i-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1	2-7 1
DLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	1	1	1	1	2	2	2	2	1	1
	9000pm	0	0	0	0	3	3	5	3	4	6	6	4	2	1
UBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	mqq0006	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	9000ppm	0	0	0	0	0	0	1	0	1	0	2	1	0	0

(IIAN190)

BAIS 2

APPENDIX A 1-3

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO.: 0223

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE: 1

linical sign	Group Name	Admini	stration We	ek-day _											
		1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	24	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	٥
1 DOBNEOT FOR	1778ppm	0	0	0	0	0	0	0	0	0	0	0	. 0	0	0
	2667ppm	0	n	0	0	0	n	n	0	0	n	0	0	0	0
	4000ppm	0	0	0	0	n	0	0	0	0	n	0	0	n	0
	6000ppm	0	0	0	0	0	0	0	0	0	. 0	0	n	0	0
	9000ppm	0	0	0	0	0	0	0	. 0	0	1	1	1	1	1
	00000	Ü	v	•	V	ν,	v	U	V	V		1	•	1	1
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	mqq0006	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
1.1G0-ST001.	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	mqq0000	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000pm	0	0	0	0	1	1	1	1	1	1	1	1	1	1

(HAN190)

BAIS 2

APPENDIX A 1-4

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO.: 0223

SEX : FEMALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

W. 111P • W. P

PAGE: 2

Clinical sign	Group Name	Admini	stration We	eek-day											
		1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SMALL STOOL	Control	0	0	0	Λ	0	n	0	. 0	0	0	0	0	0	0
OTOOL	1778ppm	0	0	0	0	0	ñ	0	0	0	0	0	0	0	0
	2667ppm	0	Ô	0	0	Õ	Õ	Ö	0	0	Ô	Ö	0	0	0
	4000ppm	0	Ö	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000pm	0	0	0	0	1	1	0	0	0 .	0	0	0	0	0
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0 -	0	0	0	0	0
	1778ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2667ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	9000ppm	0	0	0	0	1	1	0	0	0	0	0	0	0	0

(HAN190)

BAIS 2

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0222

ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 1

oup Name	Admini	stratio	on week-day											
	0-0		1-1		1-2		1-4		1-7		2-3		2-7	
Control	128±	5	133±	5	136±	5	143土	5	154±	7	166±	8	178±	10
1778ppm	128±	5	128±	4	132±	4	139±	3	149±	3	160±	4	170±	5
2667ppm	128±	4	126±	4**	128±	5**	134±	5**	144±	6	155±	7	165士	8*
4000pm	128±	5	124±	5**	121±	5**	121±	7**	129士	9**	139±	10**	149±	11**
6000ppm	128±	5	121±	5**	116±	5**	110±	7**	109士	11**	113±	15**	122±	14**
9000pm	128±	5	119±	5**	111±	4**	100±	5**	87±	9**	79±	12**	85±	13**
Significant differe	nce; *: P ≦	0.05	**: P ≤ 0.01	l			Test of Du	nnett						

(HAN260)

BAIS 2

APPENDIX A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0222

ANIMAL : RAT F344

UNIT : g REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2

oup Name	Admini	stratio	n week-day											
	0-0		1-1		1-2		1-4		1-7		2-3		2-7	
Control	106±	4	109±	4	110±	5	112±	5	119±	5	124±	5	129±	6
1778ppm	106±	4	105±	4	107±	4	111土	4	117±	4	122±	5	126士	5
2667ppm	106±	4	103±	4*	104土	5*	108生	5	112±	6	118±	7	122±	8
4000ppm	106±	4	101±	4**	98±	4**	100士	5**	106±	6**	111±	6*	116±	6**
6000ppm	106±	4	99±	4**	94±	4**	89±	6**	89±	9**	91±	14**	103土	10**
9000ppm	106±	4	93±	4**	91土	4**	82±	3**	70±	5**	64±	2**	68生	0 ?
Significant differe	nce; *:P≦0	.05	**: P ≤ 0.0	1			Test of Du	nnett						

^{?:} Significant test is not applied, because No. of data in this group is less than 3.

(HAN260)

BAIS 2

APPENDIX A 2-3

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0223

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

p Name	Λdministration	week-day					
	0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	23.6± 0.8	23.1± 1.0	23.4± 1.0	23.9± 1.2	24.0± 1.2	24.0生 1.2	24.5± 1.2
1778ppm	23.6± 0.9	23.1± 0.8	23.4± 0.7	24.0± 0.6	24.4± 0.6	24.4± 0.7	24.7± 0.8
2667ppm	23.6± 0.9	22.7± 1.0	22.9± 1.2	23.6± 1.1	24.0± 1.2	23.7± 1.2	24.1± 1.4
4000ppm	23.6± 0.9	22.3± 0.9	22.4± 1.0	23.2± 1.2	23.6± 1.1	23.7± 1.4	24.0± 1.1
6000ppm	23.6± 0.9	21.6± 0.7**	21.6± 0.6**	22.4± 0.6**	22.9± 0.8	23.2± 0.8	23.3± 0.8
mqq0000	23.6生 0.8	21.3± 0.7**	20.7士 0.7**	20.9± 1.2**	21.4士 2.0**	21.7± 2.4**	21.7± 2.7**
Significant differenc	o · * · P < 0.05	** : P ≤ 0.01		Test of Dunnett			<u></u>
Significant uniterend	8, ↑, 1 ≥ 0.00	** · l ≥ 0.01		Test of Darkett			

PAGE: 1

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO.: 0223

ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2

oup Name	Administration	week-day					
	0-0	1-1	1-2	1-4	1-7	2-3	2-7
Control	18.9± 0.6	18.6± 0.5	18.4± 0.3	19.0± 0.5	19.1± 0.3	19.4± 0.5	19.8± 0.5
1778ppm	18.9± 0.8	18.2± 0.7	18.5± 0.6	18.7± 0.7	19.1± 0.8	19.3± 1.1	19.6± 0.8
2667 ppm	18.9± 0.8	17.7± 0.7*	17.8± 0.8	18.4± 0.8	18.9± 0.7	18.8± 0.8	19.2± 0.9
4000ppm	18.9± 0.6	17.6± 0.7**	17.6± 0.8*	18.6± 0.8	18.9± 0.8	19.0± 0.9	19.4± 0.9
6000ppm	18.9± 0.8	16.9± 0.8**	16.6± 0.6**	17.5± 0.7**	18.3± 0.8*	18.8± 0.6	18.9± 0.6*
9000ppm	· 18.9± 0,6	16.6± 0.6**	15.8± 0.4**	16.2生 0.6**	17.1± 0.7**	17.9± 0.8**	18.3士 0.6**
						777	
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
AN260)					· · · · · · · · · · · · · · · · · · ·		

APPENDIX A 3-1

WATER CONSUMPTION CHANGES : SUMMARY, RAT: MALE (TWO-WEEK STUDY)

STUDY NO. : 0222

ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2

SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Name	Administration 1–3(3)	week-day(effective) 1-7(4)	2-3(3)	2-7(4)	
ontrol	16.5± 1.7	16.7± 2.9	17.8± 3.6	16.6± 3.6	
778ppm	11.8± 0.8	11.4± 0.6	12.7± 0.8	10.6± 0.6	
667ppm	10.2± 1.2	10.8± 1.0*	12.5± 1.5*	10.0± 1.1**	
Mqq000	7.4± 1.2**	10.0± 0.4**	11.6± 0.7**	9.2± 0.4**	
:000ppm	4.6± 0.6**	6.6± 2.2**	9.9± 2.5**	9.2± 1.3**	
maq0000	2.8± 0.4**	2.8± 0.5**	4.9± 1.6**	4.6生 0.0 ?	
ignificant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett	

^{?:} Significant test is not applied, because No. of data in this group is less than 3.

(IIAN260)

BAIS 2

PAGE: 2

APPENDIX A 3-2

WATER CONSUMPTION CHANGES : SUMMARY, RAT: FEMALE (TWO-WEEK STUDY)

STUDY NO.: 0222

ANIMAL : RAT F344 UNIT : g

REPORT TYPE : A1 2

SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Group Name Administration week-day(effective)_ 1-3(3)1-7(4)2 - 3(3)2-7(4)Control 17.8± 1.0 17.9± 1.3 19.4士 1.6 18.7± 1.4 1778ppm 13.5± 0.9** 15.2± 1.1** 13.6士 0.8** 2667ppm 11.4生 0.5** 13.5± 1.0** 14.3± 1.1** 12.9生 1.0** 4000ppm 7.7± 1.2** 11.1± 2.0** 13.8土 1.5** 12.3± 1.8** 6000ppm 4.6± 0.7** 6.3± 1.7** 9.1± 2.1** 9.0± 0.9** 9000ppm 3.1士 0.6** 3.1± 1.3** 3.7生 1.5** 4.8± 1.2** Significant difference; $*:P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett (IIAN260)

BAIS 2

PAGE: 1

APPENDIX A 3-3

WATER CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE (TWO-WEEK STUDY)

STUDY NO.: 0223

ANIMAL : NOUSE BDF1

UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration	week-day(effective)				
	1-3(3)	1-7(4)	2-3(3)	2-7(4)		
Control	3.9± 0.3	4.0± 0.4	3.9± 0.2	3.9± 0.4		
1778ppm	3.2± 0.2	3.2± 0.2	3.1± 0.4	3.0± 0.5		
2667ppm	2.6± 0.3*	2.8± 0.2*	2.5± 0.2*	2.5生 0.4*		
4000pm	2.1± 0.3**	2.4± 0.3**	2.1± 0.3**	2.0± 0.3**		
6000ppm	1.5士 0.2**	2.1± 0.2**	1.8± 0.1**	1.7± 0.2**		
9000pm	1.0± 0.1**	1.7± 0.4**	1.5± 0.3**	1.5± 0.2**		
			-			
Significant differe	ence; *: P ≤ 0.05	** : P ≦ 0.01		Test of Dunnett		
IAN260)					 	BAIS

APPENDIX 3-4

WATER CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE

(TWO-WEEK STUDY)

STUDY NO.: 0223

ANIMAL : NOUSE BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration	week-day(effective)_			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)	
Control	4.3± 0.3	4.5± 0.3	4.5± 0.4	4.5± 0.3	
1778ppm	3.1± 0.4	3.1± 0.4**	3.2± 0.3**	3.2± 0.4	
2667ppm	2.6± 0.2	2.8± 0.2**	2.8± 0.2**	2.7± 0.2	
4000ppm	2.1± 0.1**	2.7± 0.2**	2.4± 0.2**	2.4± 0.2**	
Mqq0000	1.4士 0.1**	2.2± 0.2**	2.1± 0.2**	1.7士 0.1**	
9000pm	0.9± 0.1**	1.8± 0.2**	1.8± 0.2**	1.8± 0.3**	
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett	

APPENDIX A 4-1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE
(TWO-WEEK STUDY)

STUDY NO. : 0222

ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration	week-day(effective)	· · · · · · · · · · · · · · · · · · ·	 	
	1-7(7)	2-7(7)	,		
Control	13.8± 1.1	14.9± 1.2			
1778ppm	12.5± 0.5*	13.8± 0.6			
2667ppm	11.8± 0.6**	13.6± 0.8*			
4000ppm	9.3± 1.3**	12.3± 1.2**			
mqq0000	6.7± 1.0**	9.4± 1.5**			
9000pm	4.3± 0.9**	5.7± 1.2**			
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01	Test of Dunnett		
IAN260)				 BAI	

PAGE: 1

APPENDIX A 4-2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0222

ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2

SEX: FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)

PAGE: 2

ALL ANIMALS

up Name	Administration 1-7(7)	week-day(effective) 2-7(7)			
Control	11.0± 0.8	11.2± 1.0			
1778ppm	10.2± 0.5	11.0± 0.7			
2667ppm	9.2± 0.7	10.6± 1.1			
4000ppm	7.7± 0.7**	10.0± 0.7*			
6000ppm	5.1± 1.0**	8.5± 1.3**			
9000ppm	3.3± 0.3**	5.0± 0.0 ?			
Significant difference	ce; *: P ≤ 0.05	** : P ≤ 0.01	Test of Dunnett		

APPENDIX A 4-3

FOOD CONSUMPTION CHANGES: SUMMARY, MOSUE: MALE

(TWO-WEEK STUDY)

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

SEX : MALE				PAGE:
roup Name	Administration 1–7(7)	week-day(effective) 2-7(7)		
Control	3.5± 0.3	3.6± 0.3		
1778ppm	3.5± 0.2	3.6± 0.2		
2667ppm	3.4± 0.3	3.5± 0.2		
4000ppm	3.2± 0.2	3.5± 0.3		
6000ppm	3.1± 0.2**	3.5士 0.2		
9000ppm	2.9± 0.1**	3.5± 0.6		
	ence; *: P ≤ 0.05	** : P ≤ 0.01	Test of Dunnett	
IAN260)				BAIS 2

APPENDIX A 4-4

FOOD CONSUMPTION CHANGES: SUMMARY, MOSUE: FEMALE
(TWO-WEEK STUDY)

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

up Name	Administration	week-day(effective)	· · · · · · · · · · · · · · · · · · ·	
	1-7(7)	2-7(7)		
Control	3.2± 0.1	3.5± 0.2		
1778ppm	3.0± 0.3	3.3± 0.2		
2667ppm	2.8± 0.2**	3.2± 0.2**		
5001 pp(ii	2.O.L V.2**	0.21 0.2**		
4000ppm	2.7± 0.2**	3.1± 0.2**		
6000ppm	2.6± 0.1**	3.1± 0.2**		
9000pm	2.3± 0.2**	3.1± 0.2**		
Significant differen	ce; $*: P \le 0.05$	$**: P \leq 0.01$	Test of Dunnett	

APPENDIX A 5-1

CHEMICAL INTAKE CHANGES: SUMMARY, RAT: MALE

(TWO-WEEK STUDY)

ANIMAL : RAT F344

UNIT : mg/kg/day

REPORT TYPE : A1 2

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

Group Name	Administration	(marka)	
a och valla	1	2	
Control	0.000± 0.000	0.000± 0.000	
1778ppm	161.190± 10.745	141.687± 7.012	
2667ppm	248.546± 14.154	209.708± 10.901	
4000ppm	344.458± 40.708	330.614± 27.033	
60000m	343.547± 68.453	443.380± 56.195	
9000pm	312.579± 93.832	503.930± 98.662	
(IIAN300)			BAIS

APPENDIX A 5-2

CHEMICAL INTAKE CHANGES: SUMMARY, RAT: FEMALE

(TWO-WEEK STUDY)

ANIMAL : RAT F344

UNIT : mg/kg/day
REPORT TYPE : A1 2

SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

Group Name	Administration 1	(weeks)2	, , , , , , , , , , , , , , , , , , ,	/	
Control	0.000± 0.000	0.000± 0.000			
1778ppm	173.780± 6.369	148.622± 6.046		,	
2667ppm	257.772± 17.610	217.256± 12.508			
4000ppm	379.251± 15.156	318.364± 13.830			
6000ppm	434.232±112.501	539.051± 64.246			
9000pm	357,556± 63.374	608.823± 0.000			

(IIAN300)

BAIS 2

PAGE: 2

APPENDIX A 5-3

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE

(TWO-WEEK STUDY)

ANIMAL : MOUSE BDF1 UNIT : mg/kg/day

REPORT TYPE : A1 2

CHENICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

			PAGE:
Group Name	Administration 1	2 2	
Control	0.000± 0.000	0.000± 0.000	
1778ppm	234.124± 14.368	216.479± 34.901	
2667ppm	307.359± 17.599	276.649± 40.298	
4000ppm	400.214± 40.871	335.646± 44.561	
6000ppm	554.876± 33.224	443.647± 36.612	
maa0000	706.584±114.095	613.979± 80.015	
IIAN300)			BAI

APPENDIX A 5-4

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE (TWO-WEEK STUDY)

ANIMAL : MOUSE BDF1

UNIT : mg/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

SEX : FEMALE			PAGE:
Group Name	Administration	ueeks)	
		2	
Control	0.000± 0.000	0.000± 0.000	
1778ppm	287.564± 30.333	285.549± 38.652	
2667ppm	398.985± 18.132	379.188± 22.742	
4000ppm	566.778± 45.094	495.016± 43.414	
6000ppm	710.398± 56.520	552.528± 35.704	
9000pm	946.025± 70.351	858.567 ± 134.228	

(IIAN300)

APPENDIX A 6-1

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT: MALE

STUDY NO. : 0222 ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 1

roup Name	NO. of Animals	RED BLOOD CELL 1 O ⁶ / μ ^g		HEMOGLOBIN g∕d≬		HEMATOCRIT %		MCV f @		MCH Pg		g ∕d% g ∕d%		PLATELET 1 Ο³ / μዩ	
Control	5	8.00±	0,25	15.1±	0.6	44.6±	1.2	55.7±	0.5	18.8±	0.3	33.8±	0.8	922±	35
1778ppm	5	7.97±	0.09	15.2±	0.1	44.0±	0.8	55.3±	0.4	19.0±	0.3	34.4±	0.7	909±	37
2667ppm	5	8.13±	0.24	15.5±	0.4	45.3±	1.0	55.7±	0.5	19.1±	0.3	34.3±	0.4	907±	47
4000ppm	5	8.15±	0.23	15.4±	0.3	44.9±	1.2	55.1±	0.5	18.9±	0.3	34.4±	0.5	837±	14
6000ppm	5	8.51±	0.17	16.4±	0.5*	47.2±	1.1	55.5±	0.6	19.2±	0.4	34.7±	0.4	650±	169*
9000ppm	5	9.68±	0.85**	18.7±	1.6**	54.8±	7.0**	56.5±	2.2	19.3±	0.1	34.3±	1.3	304±	162**

(IICL070)

STUDY NO.: 0222 ANIMAL : RAT F344

REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (2)

(IICL070)

oup Name	NO. of Animals	RETICUL	OCYTE	PROTHRO s e c	MBIN TIME	APTT sec	
Control	5	48±	6	12.7±	0.5	19.3±	2.3
1778ppm	5	41±	10	12.8±	0.3	19.4±	2.7
2667ppm	5	40±	13	12.7±	0.5	20.8±	2.0
4000ppm	5	38±	4	12.9±	0.8	21.2±	2.3
6000ppm	5	21±	12**	13.5±	0.3	20.3±	2.6
9000pm	5	11±	7**	15.3±	0.0 ?	23.3±	0.0 ?
Significant	difference;	*: P ≤ 0	.05	**: P ≤ 0.0)1		Test of Dunnett
?:Signifi	cant test is no	ot applied,b	ecause No.	of data in 1	this group is	less than	3.

PAGE: 2

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 1

oup Name	NO. of Animals	WBC 1 O³∕µ₽			Differential WBC N-BAND		(%) N-SEG		EOSINO		BASO		момо		LYMPHO		OTHERS	
Control	5	6.20±	1.47	0±	0	15±	4	1±	1	0±	0	3±	2	81±	4	0±	C	
1778ppm	5	4.99±	0.65	0±	0	13±	2	1 ±	1	0±	0	2±	1	84±	2	0±	(
2667ppm	5	5,25±	0.97	0±	1	12±	4	1 ±	1	0±	0	3±	1	83±	1	0±	C	
4000ppm	5	4.89±	1.26	0±	0	14士	2	1±	0	0 ±	0	4±	1	81土	2	0±	C	
6000ppm	5	5.04±	1.62	0±	0	20±	5	1±	i	0±	0	4±	1	75±	6	0±	(
9000ppm	5	3.44±	0.71**	0±	0	29±	10	2±	2	0土	0	4±	1	66±	10	0±	(
Significan	t difference ;	*:P≦	€ 0.05	**: P ≦	0.01			Test	af Dunne	rtt								
CL071)																	BAIS	

APPENDIX A 6-2

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT: FEMALE

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

SEX : FEMALE

roup Name	NO. of Animals	RED BLOOD CELL 1 O ⁶ /µl	∥EMOGLOBIN g∕dl	HEMATOCRIT %	MCV f ℓ	MCII Pg	g ∕q _l WCIIC	PLATELET 1 O³ / μλ	
Control	5	8.29± 0.21	15.7± 0.4	46.0± 1.0	55.6± 0.3	19.0± 0.5	34.2± 0.9	919± 34	
1778ppm	5	8.28± 0.11	16.2± 0.3	46.0± 0.7	55.5± 0.3	19.5± 0.3	35.2± 0.4	821± 66	
2667ppm	5	8.44± 0.25	16.3± 0.6	46.5± 1.4	55.1± 0.4	19.4± 0.2	35.1± 0.3	758± 75*	
4000ppm	5	8.21± 0.18	15.9± 0.5	45.1± 1.2	54.9± 0.4*	19.4± 0.5	35.3± 1.1	729± 101*	
6000ppm	5	8.46± 0.18	16.1± 0.4	46.5± 0.8	55.0± 0.4	19.0± 0.5	34.6± 0.8	665± 140**	
maq0000	0	-	-	-	-	- -	-	~	
Significant	difference;	*: P ≤ 0.05 *	**: P ≤ 0.01		Test of Dunnett				

(IICL070)

BAIS 2

PAGE: 3

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (2)

SEX : FEMALE

Group Name	NO. of Animals	RETICUL ‰	OCYTE	PROTHRO sec	MBIN TIME	APTT sec		
Control	5	28±	7	13.2±	0.6	20.0±		
1778ppm	5	27±	8	12.9±	0.2	18.5±		
2667ppm	5	28±	4	13.3±	0.7	21.9±		
4000ppm	5	32±	5	13.7±	0.8	21.2±		
6000pm	5	29±	10	13.9±	0.4	18.7±		
9000ppm	0	-		-		-		
Significant	t difference;	*: P ≤ 0	.05	** : P ≤ 0.0	1		Test of Dunnett	
(HCL070)					-··· · · · · · · · · · · · · · · · · ·			 BAISS

PAGE: 4

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 2

roup Name	NO. of Animals	WBC 1 Of	; } / µ.g		Differential WBC (%) N-BAND N-SEG			EOSTNO		BASO		MONO		LYMPHO		OTHERS	
Control	5	4.43±	0.65	0±	0	15±	5	2±	1	0±	0	4±	i	80士	4	0±	(
1778ppm	5	4.17±	1.27	0±	1	15±	4	2±	1	0 ±	0	4±	2	79±	7	0±	1
2667ppm	5	5.25±	1.28	0±	0	12±	1	2±	1	0 ±	0	· 3±	1	84±	2	0±	0
4000ppm	5	5.01±	1.31	0±	0	15±	4	1±	1	0 ±	0	3±	1	81±	2	0 ±	0
6000ppm	5	4.20±	1.42	0±	0	28士	12	2土	1	0±	0	3±	1	67土	12	0±	0
9000pm	0	-		-				-		-		-		-		-	
Significan	t difference ;	* : P <u>s</u>	≦ 0.05	**: P ≦	0.01			Test	of Dunne	tt							

(HCL071)

APPENDIX A 6-3

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 1

oup Name	NO. of Animals	RED BL	ITS OOD CEI'T	HEMOGLO g / dl		HENATOO %	CRIT	MCV f e		MCII Pg		MCIIC g∕d1		PLATELI 1 0°/1	
Control	5	10.53±	0.25	15.8±	0.3	47.6±	1.3	45.1±	0.3	15.0±	0.2	33.2±	0.5	1373±	122
1778ppm	5	10.36±	0.12	15.5±	0.2	46.9±	1.0	45.3±	0.6	15.0±	0.2	33.1±	0.5	1258±	99
2667ppm	5	10.69±	0.52	16.2±	0.6	48.4±	2.4	45.3±	0.7	15.1±	0.2	33.4±	0.5	1273±	114
4000ppm	5	10.57±	0.22	15.9±	0.2	47.8±	1.2	45.3±	0.7	15.0±	0.2	33.2±	0.5	1238±	28
6000ppm	5	10.73±	0.37	16.3±	0.4	47.9±	1.3	44.7±	0.9	15.2生	0.3	34.0±	0.1*	1214±	42
9000ppm	5	11.29±	0.45*	17.1±	0.7**	51.3±	2.5*	45.4±	1.0	15.2±	0.2	33.4±	0.4	1270±	91
Significant	difference;	*: P ≤ (0.05 *	* : P ≤ 0.0	1			Test of Dur	nett					- W. 11	

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (2)

SEX : MALE

roup Name	NO. of Animals	WB(1 O	C ³∕μℓ		fferentia BAND		6) SEG	EO	SINO	BAS	50	non	10	LY	MPHO	OTI	HERS
Control	5	2.23±	1.05	0±	0	14±	9	2±	2	0±	0	3±	1	82±	11	0±	(
1778ppm	5	2.07±	0.76	1±	0	11±	3	2±	1	0±	0	3±	1	84±	3	0 ±	(
2667ppm	5	3.01±	1.04	1±	1	12±	4	2±	1	0 <u>+</u>	0	2±	1	83±	5	0±	C
4000ppm	5	2.21±	0.71	0±	1	12±	1	2±	2	0±	0	2±	2	84±	2	0±	C
6000ppm	5	1,97±	0.58	0±	0	10±	2	1±	1	0±	0	2±	2	86±	4	0 ±	0
9000pm	5	1.87±	1.62	3±	7	19±	20	2±	1	0±	0	3±	1	73±	26	0士	0
Significant	difference;	*: P ≦	≦ 0.05	**: P ≦	0.01			Test	of Dunne	tt							

APPENDIX A 6-4

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO.: 0222
ANIMAL: RAT F344
REPORT TYPE: A1
SEX: MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: I

oup Name	NO. of Animals	TOTAL P g/dl	ROTEIN	ALBUMIN g∕dl	i	A/G RAT	.10	T-BILI mg∕dl		GLUCOSE mg∕dl		T-CHOLE mg/al	STEROL	PHOSPHOI mg/dl	JPID
Control	5	6.0±	0.1	3.6±	0.1	1.5±	0.1	0.35±	0.07	190±	11	61±	2	124±	5
1778ppm	5	5.9±	0.1	3.5±	0.1	1.5±	0.0	0.34±	0.08	190±	6	53±	2	105±	5
2667ppm	5	5.9±	0.1	3.5±	0.1	1.5±	0.0	0.33±	0.14	205±	17	52±	3	99±	7
4000ppm	5	5.9±	0.1	3.5±	0.1	1.5±	0.1	0.39±	0.06	193±	16	53±	3	97±	5*
6000ppm	5	5.7±	0.3	3.6±	0.2	1.6±	0.1*	0.51±	0.10	167±	33	57±	12	86±	10**
9000pm	5	5.3±	0.3**	3.3±	0.2	1.7±	0.2*	0.39±	0.12	115±	39*	58±	18	73±	22**

(HCL074)
BAIS 2

STUDY NO.: 0222
ANIMAL: RAT F344

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

REPORT TYPE : A1
SEX : MALE

PAGE: 2

oup Name	NO. of Animals	GOT I U / @		GPT IU/e		LDII IU/0		G-GTP IU/e		CPK I U / 0		UREA NITROGEN mg∕d2	CREATININE mg/dl
Control	5	57±	2	21±	2	221±	44	1±	0	168士	20	17.1± 1.1	0.4± 0.1
1778ppm	5	53±	4	11±	2*	164土	20	1±	0	125±	5	20.1± 3.2	0.4± 0.1
2667ppm	5	54±	3	10±	1**	203±	40	1±	0	174±	45	19.8± 2.7	0.4± 0.1
4000ppm	5	55±	3	10±	2**	199±	39	1±	0	177±	37	20.1± 2.7	0.4± 0.1
6000ppm	5	66±	14	11±	2*	243±	60	1±	0	195±	40	23.7± 6.7*	0.3± 0.1
9000ppm	5	123±	81	20±	12	242±	68	1±	1	185±	31	33.7± 16.9**	0.3± 0.0

(IICL074)

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1

BICCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : MALE

PAGE: 3

oup Name	NO. of Animals	SODIUM meq/e	?	POTASSII mEq/l		CHLORID mEq/l		CALCIUM mg/dl		INORGAN mg∕dl	HC PHOSPHORUS	
Control	5	142±	1	4.2±	0.3	105士	1	10.9±	0.1	8.7±	0.8	
1778ppm	5	141±	2	4.3±	0.3	107生	1	10.9±	0.2	6.8±	1.8	
2667ppm	5	142±	1	3.9±	0.4	107±	1	10.9±	0.2	6.5±	1.2	
4000ppm	5	142±	2	3.9±	0.6	107土	1	11.1±	0.6	6.3±	1.2	
6000ppm	5	143±	2	3.6±	0.1	108士	2	11.2±	0.2	4.9±	1.0**	
9000pm	5	158±	17*	3.5±	0.3*	124士	19**	10.1±	0.5*	6.6±	2.1	

APPENDIX A 7-1

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT: MALE

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX: FEMALE

NEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 2

roup Name	NO. of Animals	RED BLO	OOD CELL	HEMOGLO g∕dl	DBIN	IIENATOO %	CRIT	MCV F @		MCII pg		MCIIC g∕dl		PLATELE 1 O³/μ	
Control	5	9.87±	0.66	15.3±	0.7	44.5±	2.2	45.1±	0.7	15.5±	0.4	34.3±	0.4	1003±	55
1778ppm	5	9.95±	0.26	15.2±	0.2	44.4±	0.8	44.6±	0.8	15.3±	0.3	34.3±	0.3	1080±	81
2667ppm	5	9.80±	0.45	15.1±	0.5	44.0±	1.8	44.9±	0.5	15.4±	0.3	34.4±	0.6	1047士	145
4000ppm	5	10.05±	0.23	15.2±	0.4	44.5±	0.8	44.3±	1.0	15.2±	0.4	34.2±	0.5	1138士	74
6000ppm	5	10.13±	0.43	15.8±	0.7	45.8±	2.1	45.2±	0.8	15.6±	0.1	34.5±	0.6	1052±	47
9000ppm	5	10.40±	0.38	16.0±	0.6	46.7±	1.8	44.9±	0.9	15.4±	0.2	34.2±	0.6	1027±	84
Significant	difference;	*: P ≦ (0.05	** : P ≦ 0.0	1			Test of Dur	nnett	***************************************			*****		
ICL070)								······································							

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 2

MBC □ O3 / μℓ	ame NO. of Animals	Dif N-B	ferentia AND	L WBC (% N-S		EOS	SINO	BAS	50	MON	10	LYN	IPHO	011	HERS
± 1.00	tral 5	0±	1	10 : L	3	1±	1	0±	0	3±	1	86±	4	0±	0
± 0.51	3ppm 5	0 ±	0	11±	2	2±	1	0±	0	2±	1	85±	2	0±	0
± 0.82	opm 5	0土	0	8±	2	2±	1	0 ±	0	2±	1	88土	3	0±	0
± 0.78)ppm 5	ī±	1	12±	2	3±	2	0±	0	3±	1	82±	2	0±	0
土 1.04)ppm 5	0±	1	11±	3	2±	2	0±	0	2±	1	84士	6	0 ±	0
± 2.22	7 maa	0±	0	11±	1	2±	1	0±	0	3±	2	84±	3	0±	0
P ≤ 0.05	nificant difference	** : P ≤ (0.01			Test	of Dunne	tt							
P ≤ 0.05	nificant difference	** : P ≦	<u> </u>	0.01	5 0.01	5 0.01	5 0.01 Test	5 0.01 Test of Dunne	5 0.01 Test of Dunnett						

APPENDIX A 7-2

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT: FEMALE

STUDY NO.: 0222
ANIMAL: RAT F344
REPORT TYPE: A1
SEX: FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 4

oup Name	NO. of Animals	TOTAL F g/dl	PROTEIN	g∕d% ALBUMIN		A/G RAT	10	T-BILI mg∕d£		GLUCOSE mg/dl		T-CHOLES mg∕dl	STEROL	PHOSPHO mg/dl	LIPID
Control	5	5.8±	0.0	3.5±	0.1	1.5±	0.1	0.46±	0.13	196±	13	66±	2	120±	6
1778ppm	5	5.7±	0.1	3.5±	0.1	1.6±	0.0	0.49±	0.10	196±	18	57±	7	103±	14
2667ppm	5	5.7±	0.2	3.5±	0.1	1.6±	0.1	0.47±	0.08	188生	9	53±	7**	92±	12**
4000ppm	5	5.6±	0.1	3.5±	0.1	1.7±	0.1*	0.41±	0.08	192±	9	49±	3**	83±	7**
6000ppm	5	5.8±	0.2	3.6±	0.1	1.7±	0.1**	0.36±	0.06	155±	20**	51±	7**	78±	9**
9000pm	0	-		· -		-		-		_		-		-	

(IICL074)

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 5

oup Name	NO. of Animals	GOT IU/0		GPT IU∕ℓ		LDII I U /	?	G-GTP IU/e		CPK IU/e		UREA NI mg∕⊲l¢		CREATIA mg∕⊲l¢	
Control	5	61±	3	19±	2	231±	37	2±	0	151 ±	34	18.1±	3.0	0.4±	0.0
1778ppm	5	57±	5	10±	2**	255±	90	1±	1	133±	22	22.0±	2.1	0.4±	0.1
2667ppm	5	63±	2	10±	1**	254±	98	1土	1	143±	28	22.2±	2.9	0.3±	0.1
4000ppm	5	79±	40	20±	21	359±	389	2±	0	156±	29	22.4±	2.7	0.3±	0.0
6000ppm	5	70±	7*	12±	3	279±	77	1±	1	188士	36	22.8±	3.8	0.3±	0.0
9000pm	0	-		-		_		_		-		-		_	

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 6

roup Name	NO. of Animals	SODIUM mEq/e	POTASSIUM mEq∕ℓ	CHLORIDE mEq∕ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg∕d¢	
Control	5	142± 1	3.7± 0.4	107± 2	10.9± 0.7	7.4± 1.2	
1778ppm	5	141± 1	3.6± 0.2	107± 1	10.5± 0.2	6.4± 1.4	
2667ppm	5	142± 1	3.6± 0.1	108± 1	10.4± 0.1	5.9± 1.1	
4000ppm	5	141± 1	3.8± 0.3	109± 1	10.4± 0.1	5.8± 1.2	
6000ppm	5	142± 1	4.3± 0.3*	108± 1	11.1± 0.5	5.5± 0.6	
9000ppm	0	-	-	-	-	-	
Significant	difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett		

(IICL074)

APPENDIX A 7-3

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 1

roup Name	NO. of Animals	I ATOT g / dg	PROTEIN	g ∕dl dLBUNIN		A/G RAT	10	T-BILI mg/clf		GLUCOSE mg/cl2		T-CHOLE	STEROL	GOT IU/6)
Control	5	5.4±	0.4	3.0±	0.1	1.2±	0.2	0.29±	0.04	306±	33	97土	13	32士	1
1778ppm	5	5.2±	0.2	2.9±	0.1	1.3±	0.1	0.26±	0.08	317±	10	77±	4*	33±	4
2667ppm	5	5.4±	0.4	3.0±	0.2	1.2±	0.1	0.30±	0.11	286±	29	83±	18	34±	3
4000pm	5	5.1±	0.1	2.8±	0.0	1.2±	0.1	0.30±	0.15	292±	22	77±	4*	33±	4
6000pm	5	5.0±	0.2	2.8±	0.1	1.3±	0.1	0.25±	0.09	285±	20	75±	6*	33±	2
9000pm	5	5.4±	0.5	3.1±	0.4	1.3±	0.1	0.34±	0.13	235±	59	80±	8	53±	34
Significant	difference;	*: P ≦ ().05	**: P ≤ 0.0)1	***		Test of Du	nnett			*****			

(IICL074)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 2

oup Name	NO. of Animals	GPT IU/e		LDH IU/0		CPK I U / 0		UREA N mg∕dl	ITROGEN	SODIUM mEq/l		POTASS mEq/		CHLORIDI mEq/l	
Control	5	15±	1	208±	91	41±	15	25.1±	2.9	150±	3	4.8士	0.6	117士	3
1778ppm	5	12±	2	202±	49	60士	43	22.5±	1.7	150土	1	4.5±	0.5	119土	2
2667ppm	5	11±	2	213±	84	45±	15	26.4±	5.6	151士	1	4.7±	0.5	117±	1
4000ppm	5	13±	2	198±	55	45±	22	25.2±	4.8	150±	3	4.4±	0.4	116±	3
6000ppm	5	10±	2	187±	18	32±	5	28.0±	1.6	150土	2	4.2±	0.5	117±	1
9000ppm	5	14±	7	269±	91	85±	61	38.2±	16.0	162±	20	4.6±	0.6	123±	10

(IICL074)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 3

Group Name	NO. of Animals	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg∕dl		
Control	5	9.6± 0.	9 7.6± 1.1		
1778ppm	5	9.3± 0.	2 8.0± 1.0		
2667ppm	5	9.6± 0.	5 8.6± 2.3		
4000ppm	5	9.2± 0.	2 8.0± 2.0		
6000ppm	5	9.1± 0.	2 7.4± 1.5		
9000ppm	5	9.5± 0.	5 7.3± 0.9		
Significant	t difference;	*: P ≤ 0.05	** : P ≤ 0.01	Test of Dunnett	
(IICL074)					 RAIS 2

APPENDIX A 7-4

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 4

oup Name	NO. of Animals	TOTAL F g/dl		ALBUMIN g∕dl		A/G RAT	.10	T-BILI mg/dl		GLUCOSE mg/dl		T-CHOLE mg/dl	STEROL	GOT IU/@	
Control	5	5.2±	0.2	3.1±	0.1	1.5±	0.0	0.29±	0.06	270±	20	76±	5	42±	2
1778ppm	5	5.0±	0.1	3.0±	0.2	1.5±	0.1	0.29±	0.12	274±	35	60±	3**	44±	7
2667ppm	5	5.0±	0.1	3.1±	0.1	1.6±	0.1	0.33±	0.09	272生	25	62±	10*	36±	5
4000ppm	5	5.1生	0.1	3.1±	0.0	1.6±	0.1	0.35±	0.12	261±	24	65±	5 .	41±	8
6000pm	5	5.1±	0.2	3.0±	0.1	1.5±	0.1	0.34±	0.12	264±	17	69土	10	41 土	4
9000pm	5	5.2±	0.2	3.1±	0.1	1.5土	0.1	0.30±	0.15	264±	27	70±	5	57±	33
Significant	t difference;	*: P ≤ 0	0.05	**: P ≤ 0.0	1			Test of Du	nnett						
L074)															

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 5

TOUP Name	NO. of Animals	GPT IU/0		LDN IU/0		CPK IU/	e	UREA N mg∕dl		SODIUM mEq/l		POTASS mEq/		CliLORIDI mEq∕ℓ	
Control	5	12±	4	253±	83	69±	36	23.0±	3.5	151±	2	4.7±	0.6	118±	3
1778ppm	5	14±	3	226±	23	66±	44	24.4±	2.2	149±	2	4.5±	0.2	118±	3
2667ppm	5	11±	2	197±	28	42±	20	26.6士	2.4	150±	2	4.5±	0.3	118±	2
4000ppm	5	11±	3	234±	96	39±	12	27.9±	7.5	149±	1 .	4.8±	0.1	119±	1
6000ppm	5	11±	1	236±	30	53±	27	29.5±	4.3	153±	3	4.6±	0.2	118±	1
9000ppm	5	16±	10	316±	113	106±	109	36.6±	7.0**	156±	5*	5.4±	0.3*	116土	3
Significant	difference;	*: P ≤ 0	.05	** : P ≤ 0.03	 [Test of Dur	nnett						
ICL074)															

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 6

Group Name	NO. of Animals	CALCIUM mg/dl		INORGANIC PHOSPHORUS		
Control	5	9.0± 0	.4	7.9± 1.2		
1778ppm	5	8.9± 0	.3	8.2± 0.6		
2667ppm	5	9.0± 0	.4	7.8± 1.2		
4000ppm	5	9.0± 0	.3	7.5± 1.4		
mqq0000	5	9.1± 0	.2	8.3± 1.0		
9000pm	5	9.0± 0	.3	8.8± 1.7		
Significant	t difference;	*: P ≤ 0.05	**	:: P ≤ 0.01	Test of Dunnett	
IICL074)						 BAICO

APPENDIX A 8-1

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), ABSOLUTE

RAT: MALE

STUDY NO.: 0222 ANIMAL : RAT F344

REPORT TYPE : A1 SEX : MALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 1

oup Name	NO. of Animals	Body	Weight	ТПҮМ	US	ADRE	NALS	TEST	ES	HEAR'	ľ	LUNG	S
Control	5	173±	7	0.378±	0.029	0.042±	0.009	1.997±	0.143	0.622±	0.039	0.767±	0.023
1778ppm	5	172±	3	0.384±	0.027	0.038±	0.004	2.085±	0.149	0.601±	0.038	0.780±	0.038
2667ppm	5	166±	6	0.364±	0.027	0.040±	0.005	2.076±	0.151	0.574±	0.038	0.756士	0.047
4000ppm	5	147±	11	0.313±	0.011	0.043±	0.010	1.833±	0,258	0.533±	0.044*	0.722±	0.039
6000ppm	5	119±	19*	0.191±	0.079*	0.037±	0.005	1.498±	0.514*	0.432±	0.054**	0.614±	0.047**
9000ppm	5	85±	13**	0.057±	0.029**	0.034±	0.003	0.908土	0.211**	0.349士	0.040**	0.557±	0.014**
Significan	t difference;	*: P ≤ 0.	05 **	: P ≤ 0.01		· · · · · · · · · · · · · · · · · · ·	Test	t of Dunnett					
CL040)						 						· · · · · · · · · · · · · · · · · · ·	

(HCL040)

STUDY NO. : 0222 ANIMAL : RAT F344

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2)

REPORT TYPE: A1 SEX : MALE

UNIT: g

PAGE: 2

DUP Name	NO. of Animals	KIDI	NEYS	SPL	EEN	LIV	ER	BRA		
Control	5	1.364±	0.052	0.391±	0.026	6.672±	0.554	1.696±	.029	
1778ppm	5	1,380±	0.044	0.398±	0.030	6.699±	0.251	1.697±	.047	
2667ppm	5	1.327±	0.048	0.392±	0.020	6.491±	0.519	1.703±	.073	
4000ppm	5	1.224±	0.069	0.336±	0.039	5,478±	0.649*	1.675±	. 052	
6000ppm	5	1.101±	0.181*	0.266±	0.051**	4.280±	0.976**	1.627±	.058	
9000pm	5	0.890±	0.084**	0.165±	0.053**	2,645±	0.477**	1.587±	.052*	

APPENDIX A 8-2

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), ABSOLUTE

RAT: FEMALE

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 3

	5	130±											
1770		190∓	5	0.306±	0.013	0.046±	0.006	0.073±	0.016	0.470±	0.023	0.660±	0.017
1778ppm 5	5	126±	4	0.323±	0.017	0.044±	0.003	0.073±	0.017	0.508±	0.027	0.614±	0.023
2667ppm 5	5	119±	8	0.286±	0.019	0.043±	0.007	0.064±	0.019	0.456±	0.036	0.617±	0.032
4000ppm 5	5	114±	4**	0.279±	0.036	0.044±	0.004	0.062±	0.006	0.432±	0.022	0.623±	0.032
6000pm 5	5	103±	11**	0.193±	0.093*	0.042±	0.008	0.059±	0.011	0.372±	0.041**	0.565±	0.048**
9000ppm 1	1	68±	0 ?	0.034土	0.000 ?	0.039±	0.000 ?	0.042±	0.000 ?	0.332±	0.000 ?	0.557±	0.000 ?

^{?:} Significant test is not applied,because No. of data in this group is less than 3.

(IICL040)

STUDY NO.: 0222 ANIMAL: RAT F344

REPORT TYPE: A1
SEX: FEMALE
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 4

oup Name	NO. of Animals	KIDN	NEYS	SPL	EEN	LIV	ER	BRA	i N	
Control	5	1.046±	0.034	0.326±	0.019	4.437±	0.389	1.625±	0.046	
1778ppm	5	1.055±	0.016	0.298±	0.014	4.458±	0.254	1.597±	0.058	
2667ppm	5	1.035±	0.071	0.288±	0.024	4.080±	0.404	1.583±	0.049	
4000ppm	5	1.048±	0.015	0.277±	0.012*	3.930±	0.103	1.564±	0.033	
6000ppm	5	0.951±	0.115	0.241±	0.048**	3.549±	0.382**	1.566±	0.044	
9000ppm	1	0.853±	0.000 ?	0.135±	0.000 ?	2.717±	0.000 ?	1.499士	0.000 ?	
Significant	t difference ;	*: P ≤ 0.0	05 **:	P ≤ 0.01			Tes	t of Dunnet	t	

^{?:} Significant test is not applied, because No. of data in this group is less than 3.

(HCL040)

APPENDIX A 8-3

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), ABSOLUTE

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE: A1
SEX: MALE
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 1

oup Name	NO. of Animals	Bady Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
Control	5	24.0± 1.3	0.049± 0.008	0.012士 0.002	0.182± 0.014	0.124± 0.010	0.151± 0.021	
1778ppm	5	24.9± 0.5	0.054± 0.009	0.014± 0.004	0.153± 0.022	0.130± 0.008	0.153± 0.013	
2667ppm	5	23.8± 1.8	0.047± 0.010	0.013± 0.003	0.176± 0.031	0.126± 0.009	0.141± 0.016	
4000ppm	5	24.8± 1.1	0.054± 0.005	0.013± 0.001	0.179± 0.026	0.130± 0.011	0.154± 0.008	
6000ppm	5	23.5± 1.0	0.047± 0.008	0.014生 0.001	0.167± 0.016	0.127± 0.008	0.147± 0.012	
9000pm	5	21.0± 3.8	0.035± 0.017	0.012± 0.003	0.183± 0.019	0.114± 0.021	0.144± 0.015	
Significan	t difference ;	* : P ≤ 0.05 **	: P ≤ 0.01	Test	of Dunnett			
CL040)						•••	· · · · · · · · · · · · · · · · · · ·	

BAISZ

ANIMAL : MOUSE BDF1

REPORT TYPE : AI

SEX : MALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 2

5 5 5	0.381±	0.181 0.017 0.123	0.063± 0.057± 0.056±	0.025	1.197± 1.216±		0.446± 0.431±					
				0.007	1.216±	0.073	0.431±	0.014				
5	0.445±	0.123	0.056-4									
			0.0001	0.007	1.142±	0.208	0.445±	0.009				
5	0.404±	0.018	0.055±	0.006	1.235±	0.086	0.445±	0.010				
5	0.392±	0.039	0.052±	0.007	1.110±	0.070	0.433±	0.016				
5	0.364±	0.024	0.042±	0.016	0.984±	0.280	0.432±	0.019				
ifference;	*: P ≤ 0.05	ō **	: P ≤ 0.01	. ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		Te	est of Dunnet					
if	5	5 0.364±	5 0.364± 0.024	5 0.364± 0.024 0.042±	5 0.364± 0.024 0.042± 0.016	5 0.364± 0.024 0.042± 0.016 0.984±	5 0.364± 0.024 0.042± 0.016 0.984± 0.280	5 0.364± 0.024 0.042± 0.016 0.984± 0.280 0.432±	5 0.364± 0.024 0.042± 0.016 0.984± 0.280 0.432± 0.019	5 0.364± 0.024 0.042± 0.016 0.984± 0.280 0.432± 0.019	5 0.364± 0.024 0.042± 0.016 0.984± 0.280 0.432± 0.019	5 0.364± 0.024 0.042± 0.016 0.984± 0.280 0.432± 0.019

APPENDIX A 8-4

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), ABSOLUTE

MOUSE: FEMALE

ANIMAL : MOUSE BDF1

REPORT TYPE: A1
SEX: FEMALE
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 3

roup Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	5	19.5± 0.4	0.072± 0.006	0.015± 0.001	0.026± 0.008	0.113± 0.007	0.142± 0.011	
1778ppm	5	19.3± 1.1	0.067± 0.009	0.015± 0.001	0.025± 0.004	0.107± 0.009	0.142± 0.008	
2667ppm	5	19.0± 0.9	0.070± 0.008	0.013± 0.001	0.025± 0.005	0.105± 0.006	0.133± 0.005	
4000ppm	5	19.3± 1.1	0.069± 0.007	0.012± 0.003	0.027± 0.006	0.110± 0.007	0.140± 0.006	
6000ppm	5	18.8± 0,8	0.064± 0.006	0.012士 0.003	0.027生 0.006	0.101土 0.008	0.134± 0.006	
9000ppm	5	18.6± 0.6	0.062± 0.006	0.013± 0.003	0.026± 0.004	0.100土 0.008	0.135± 0.011	
Significan	t difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Test	of Dunnett			
ICL040)								

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX: FEMALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 4

oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN		
Control	5	0.272± 0.005	0.062± 0.009	0.923± 0.044	0.459± 0.012		
1778ppm	5	0.276± 0.020	0.058± 0.003	0.901± 0.085	0.441± 0.007		
2667ppm	5	0.279± 0.009	0.058± 0.007	0.913± 0.055	0.444± 0.023		
4000ppm	5	0.288± 0.015	0.060± 0.005	0.911± 0.086	0.444± 0.009	,	
6000ppm	5	0.287士 0.018	0.058± 0.006	0.847± 0.062	0.438± 0.007		
9000ppm	5	0.289± 0.013	0.059± 0.006	0.846± 0.026	0.430± 0.009**		
Significan	t difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Т	est of Dunnett		
CL040)							

(HCL040)

APPENDIX A 9-1

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), RELATIVE

RAT: MALE

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)
SURVIVAL, ANIMALS (2)

PAGE: 1

-aup Name	NO. of Animals		Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
Control	5	173±	7	0.218± 0.024	0.024± 0.005	1.152± 0.072	0.359± 0.014	0.443± 0.019	
1778ppm	5	172±	3	0.224± 0.015	0.022± 0.002	1.213± 0.069	0.350± 0.022	0.454± 0.021	
2667ppm	5	166±	6	0.219± 0.012	0.024± 0.003	1.251± 0.077	0.346± 0.021	0.455± 0.019	
4000ppm	5	147士	11	0.213± 0.016	0.030± 0.008	1.240± 0.108	0.362± 0.018	0.492± 0.032	
mqq0008	5	119±	19*	0.154士 0.050**	0.032± 0.002	1,231± 0.296	0.365± 0.022	0.524± 0.076	
9000pm	5	85±	13**	0.063± 0.023**	0.040± 0.005*	1.061± 0.140	0.412± 0.043*	0.662± 0.088**	
Significan	t difference;	*: P ≤ 0.	05 **	: P ≤ 0.01	Tes	t of Dunnett		t and the state of	
CL042)								**************************************	

STUDY NO. : 0222 ANINAL : RAT F344 REPORT TYPE : A1

SEX : MALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 2

JUD Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.787± 0.013	0.225± 0.014	3.843± 0.168	0.979± 0.036	
1778ppm	5	0.803± 0.029	0.232± 0.018	3.901± 0.179	0.988± 0.040	
2667ppm	5	0.800± 0.032	0.237± 0.021	3.907± 0.222	1.026± 0.024	
4000ppm	. 5	0.831 ± 0.035	0.228± 0.013	3.710± 0.215	1.140± 0.059	
6000ppm	5	0.924± 0.062**	0.222± 0.018	3.561± 0.361	1.389± 0.191*	
9000ppm	5	1.050± 0.072**	0.189± 0.035	3.088± 0.092**	1.884± 0.220**	

APPENDIX A 9-2

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), RELATIVE

RAT: FEMALE

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2)

SEX : FEMALE UNIT: %

PAGE: 3

oup Name	NO. of Animals	Body Weig (g)		TIIYMUS	ADRENALS	OVARTES	HEART	LUNGS
Control	5	130± 5	5	0.236± 0.007	0.036± 0.004	0.056± 0.014	0.363± 0.015	0.510± 0.022
1778ppm	5	126± 4	4	0.257± 0.013	0.035± 0.004	0.058± 0.015	0.404生 0.018**	0.489± 0.015
2667ppm	5	119± 8	8	0.241± 0.008	0.036± 0.004	0.054± 0.013	0.384± 0.017	0.520± 0.013
4000ppm	5	114± 4	4**	0.214± 0.026	0.039± 0.004	0.054± 0.006	0.378± 0.013	0.546± 0.034
6000ppm	5	103± 11	1**	0.182± 0.081	0.041± 0.004	0.057± 0.006	0.361± 0.022	0.549士 0.038
9000ppm	1	68± (0 ?	0.050± 0.000 ?	0.057± 0.000 ?	0.062± 0.000 ?	0.488± 0.000 ?	0.819± 0.000 ?
Significant	t difference;	*: P ≤ 0.05	**:	P ≤ 0.01	Test	of Dunnett		

(IICL042)

STUDY NO.: 0222 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 4

up Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.808± 0.021	0.252± 0.015	3.419± 0.199	1.255± 0.048	
1778ppm	5	0.841± 0.024	0.238± 0.010	3.551± 0.208	1.273± 0.072	
2667ppm	5	0.872± 0.020**	0.242± 0.007	3.428± 0.123	1.335± 0.060	
4000ppm	5	0.919± 0.025**	0.242± 0.013	3.443± 0.083	1.372± 0.063	
6000ppm	5	0.921± 0.021**	0.231± 0.028	3.439± 0.095	1.528± 0.135**	
9000ppm	1	1.254± 0.000 ?	0.199± 0.000 ?	3.996± 0.000 ?	2.204± 0.000 ?	
Significant	difference;	*: P ≤ 0.05 **:	P ≤ 0.01	Test	of Dunnett	

(HCL042)

APPENDIX A 9-3

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), RELATIVE

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 1

NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
5	24.0± 1.3	0.205± 0.033	0.051± 0.008	0.758± 0.082	0.516± 0.052	0.628± 0.067	
5	24.9± 0.5	0.216± 0.034	0.054± 0.014	0.614± 0.082	0.522± 0.029	0.615± 0.060	
5	23.8± 1.8	0.198± 0.035	0.056± 0.011	0.747± 0.167	0.532± 0.019	0.600± 0.104	
5	24.8± 1.1	0.218± 0.015	0.054± 0.006	0.721± 0.084	0.525± 0.028	0.620± 0.029	
5	23.5± 1.0	0.198± 0.027	0.061± 0.006	0.710± 0.043	0.541士 0.037	0.622± 0.036	
5	21.0± 3.8	0.157± 0.066	0.059± 0.010	0.885± 0.103	0.542± 0.030	0.697± 0.081	
t difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Tes	st of Dunnett	7 3 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		
	Animals 5 5 5 5 5 5	Animals (g) $5 24.0 \pm 1.3$ $5 24.9 \pm 0.5$ $5 23.8 \pm 1.8$ $5 24.8 \pm 1.1$ $5 23.5 \pm 1.0$ $5 21.0 \pm 3.8$	Animals (g) $5 24.0 \pm 1.3 0.205 \pm 0.033$ $5 24.9 \pm 0.5 0.216 \pm 0.034$ $5 23.8 \pm 1.8 0.198 \pm 0.035$ $5 24.8 \pm 1.1 0.218 \pm 0.015$ $5 23.5 \pm 1.0 0.198 \pm 0.027$ $5 21.0 \pm 3.8 0.157 \pm 0.066$	Animals (g) $5 24.0 \pm 1.3 0.205 \pm 0.033 0.051 \pm 0.008$ $5 24.9 \pm 0.5 0.216 \pm 0.034 0.054 \pm 0.014$ $5 23.8 \pm 1.8 0.198 \pm 0.035 0.056 \pm 0.011$ $5 24.8 \pm 1.1 0.218 \pm 0.015 0.054 \pm 0.006$ $5 23.5 \pm 1.0 0.198 \pm 0.027 0.061 \pm 0.006$ $5 21.0 \pm 3.8 0.157 \pm 0.066 0.059 \pm 0.010$	Animals (g) 5	Animals (g) 5	Animals (g) 5 24.0± 1.3 0.205± 0.033 0.051± 0.008 0.758± 0.082 0.516± 0.052 0.628± 0.067 5 24.9± 0.5 0.216± 0.034 0.054± 0.014 0.614± 0.082 0.522± 0.029 0.615± 0.060 5 23.8± 1.8 0.198± 0.035 0.056± 0.011 0.747± 0.167 0.532± 0.018 0.600± 0.104 5 24.8± 1.1 0.218± 0.015 0.054± 0.006 0.721± 0.084 0.525± 0.028 0.620± 0.029 5 23.5± 1.0 0.198± 0.027 0.061± 0.006 0.710± 0.043 0.541± 0.037 0.622± 0.036 5 21.0± 3.8 0.157± 0.066 0.059± 0.010 0.885± 0.103 0.542± 0.030 0.667± 0.081

(IICL042)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : MALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2)

PAGE: 2

OUP Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.796± 0.825	0.266± 0.112	4.988± 0.558	1.857± 0.083	
1778ppm	5	1.532± 0.097	0.227± 0.028	4.878± 0.270	1.730± 0.035	
2667ppm	5	1.902± 0.667	0.239± 0.041	4.773± 0.595	1.877± 0.135	
4000ppm	5	1.627± 0.050	0.223± 0.017	4.978± 0.312	1.794± 0.051	
6000ppm	5	1.662± 0.098	0.220± 0.022	4.717± 0.216	1.839± 0.071	
9000ppm	5	1.769± 0.266	0.191± 0.057	4.586± 0.660	2.110± 0.398	

(HCL042)

APPENDIX A 9-4

ORGAN WEIGHT (TWO-WEEK STUDY : SUMMARY), RELATIVE

MOUSE: FEMALE

ANIMAL : MOUSE BDF1

REPORT TYPE: A1
SEX: FENALE
UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 3

oup Name	NO. of Animals	Body Weight (g)	TIIYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	5	19.5± 0.4	0.367± 0.037	0.078± 0.006	0.133± 0.041	0.580± 0.040	0.729± 0.056	
1778ppm	5	19.3± 1.1	0.348± 0.050	0.079± 0.008	0.131± 0.016	0.552± 0.042	0.734± 0.042	
2667ppm	5	19.0± 0.9	0.369± 0.027	0.067± 0.007	0.133± 0.023	0.552± 0.035	0.697± 0.033	
4000ppm	5	19.3± 1.1	0.357± 0.032	0.064± 0.012	0.140± 0.030	0.568± 0.024	0.727± 0.040	
6000ppm	5	18.8± 0.8	0.339± 0.021	0.066± 0.013	0.141± 0.024	0.539± 0.041	0.714± 0.054	
9000ppm	5	18.6± 0.6	0.336± 0.039	0.068± 0.016	0.142± 0.024	0.540± 0.036	0.727± 0.039	
Significant	t difference ;	*: P ≤ 0.05 **	: P ≤ 0.01	Tes	t of Dunnett			

(HCL042)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 4

DUD Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.390± 0.044	0.317± 0.048	4.727± 0.271	2.352± 0.077	
1778ppm	5	1.425± 0.056	0.303± 0.020	4.656± 0.306	2.288± 0.161	
2667ppm	5	1.467± 0.063	0.306± 0.036	4.798± 0.198	2.338± 0.208	
4000ppm	5	1.491± 0.046*	0.311± 0.021	4.713± 0.302	2.304± 0.077	
6000ppm	5	1.522± 0.084**	0.305± 0.021	4.494± 0.257	2.327士 0.074	
9000ppm	5	1.555± 0.041**	0.316± 0.021	4.560± 0.176	2.316± 0.045	

(IICL042)

APPENDIX A 10-1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (O- 2W)

PAGE: 1

Organ	Group Name No. of Animals or Grade	Control n Study 0 1 2 3 4 (%) (%) (%) (%)	1778ppm 0 1 2 3 4 (%) (%) (%) (%)	2667ppm 0 1 2 3 4 (%) (%) (%) (%)	4000ppm 0 1 2 3 4 (%) (%) (%) (%)
[Nematopoiet	ic system]				
bone marrow	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)
	decreased hematopoiesis	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
Tymus	atrophy	(-) (-) (-) (-)	(-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-)
	karyorrhexis	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)
oleen	atrophy	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
rinary syst	tem]				
dney	vacuolic change:straight portion of proximal tubule	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-) (-)
Endacrine sy	vstem]				
drenal	hemorrhage	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-)	< 0> (-) (-) (-) (-)

STUDY NO. : 0222 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 2

DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1 : MALE

> Group Name 6000ppm 9000ppm No. of Animals on Study 0 2 2 3 4 (%) (%) (%) (%) (%) (%) (%)

[Hematopoietic system]

bone marrow

Findings

< 2> 0 2 0 0 congestion (-) (-) (-) (-) (0) (100) (0) (0)

decreased hematopoiesis 1 1 0 4 0 (-) (-) (-) (-) (50) (50) (0)

< 0> atrophy 0 0 2 0 (-) (-) (-) (0)(0)(100)(0)

karyorrhexis 2 0 0 0 (-) (-) (-) (100) (0) (0) (0)

spleen 0 1 0 0 atrophy (-) (-) (-) (-) (0) (50) (0) (0)

[Urinary system]

thymus

kidhey < 0> vacuolic change:straight portion of proximal tubule 1 1 0 0 (-) (-) (-) (50) (50) (0) (0)

[Endocrine system]

adrenal

hemorrhage 1 0 0 0 (-) (-) (-) (-) (50) (0) (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

(a) a: Number of animals examined at the site b b: Number of animals with lesion

(c) c:a/b*100 , , ,

ANIMAL : RAT F344 REPORT TYPE : A1 : MALE

SEX

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE: 3

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 0 2 3 4 (%) (%)	1778ppm 0 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	4000ppm 0 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]					
testis	atrophy	_	< 0>	< 0>	< 0>	< 0>
	an opin	(-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
pididymis	debris of spermatic elements		< 0>	< 0>	< 0>	. < 0>
	debt is at specific etements	(-) +	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
rade a > b c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: a / b * 100	3: Marked 4: Severe ne site	;			
HPT150)					- W. T. A. L.	ВЛ

STUDY NO. : 0222 ANIMAL : RAT F344

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name 6000ppm 9000ppm No. of Animals on Study 0 2 2 3 4 2 3 Findings_ (%) (%) (%) (%) (%) (%) (%) [Reproductive system] testis < 0> atrophy 1 1 0 0 (-) (-) (-) (-) (50) (50) (0) (0) epididymis < 0> debris of spermatic elements 1 0 0 0 (-) (-) (-) (50) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe a: Number of animals examined at the site <a>> b b: Number of animals with lesion (c) c:a/b*100(IIPT150) BAIS2

PAGE: 4

100

APPENDIX A 10-2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0222 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE: 5

Organ	Group Nai No. of Ai Grade	ne Control nimals on Study 0 1 2 3 4 (%) (%) (%) (%)	1778ppm 0 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	4000ppm 0 1 2 3 4 (%) (%) (%) (%)
[Nematopoi	etic system]				
bone marro	w cangestian	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	· · · · · · · · · · · · · · · · · · ·	< 0> (-) (-) (-) (-)
	decreased hematopoiesis	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
thymus	atrophy	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	<pre></pre>
	karyorrhexis	(-) (-) (-) (-)	() () ()	(-) (-) (-) (-)	(-) (-) (-) (-)
spleen	atrophy	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	karyorrhexis	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
[Urinary sy	vstem]				
kidney	mineralization:cortico-medullary junction	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> () () ()	< 0> (-) (-) (-) (-)
Grade <a> b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: a / b * 100	4 : Severe			
(IIPT150)					BAIS2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1 : FEMALE

Group Name 6000ppm 9000ppm No. of Animals on Study 1 2 Findings (%) (%) (%) [Hematopoietic system] bone marrow < 1> congestion 0 1 0 0 0 2 0 0 (0)(100)(0)(0) (0)(100)(0)(0) decreased hematopoiesis 0 1 0 0 0 2 0 , 0 (0) (100) (0) (0) (0)(100)(0)(0) thymus < 1> 〈 2〉 atrophy 0 0 2 0 0 0 1 0 (0)(0)(100)(0) (0)(0)(100)(0) karyorrhexis 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) spleen < 1> atrophy 0 1 0 0 2 0 0 0 (0) (100) (0) (0) (100) (0) (0) (0) karyorrhexis 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) [Urinary system] kidney < 1> 0 2 0 0 mineralization:cortico-medullary junction 0 0 0 0 (0)(0)(0)(0) (0) (100) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Na rked 4 : Severe

1 .

<a>>

b

(c)

a: Number of animals examined at the site

b: Number of animals with lesion

c:a/b*100

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE: 7

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 0 2 3 4 (%) (%) (%)	1778ppm 0 1 2 3 4 (%) (%) (%) (%)	2667ppm 0 1 2 3 4 (%) (%) (%) (%)	1000ppm 0 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	system]					
adrenal			< 0>	< 0>	< 0>	< 0>
	hemorrhage	(-)	(-) (-) (-)	(-) (-) (-) (-)	() (-) (-) (-)	(-) (-) (-) (-)
Grade <a> b (c)	<pre>1 : Slight 2 : Moderate a : Number of animals examined at the b : Number of animals with lesion c : a / b * 100</pre>	3 : Marked 4 : Souer site	0	ų		
(IIPT150)						BAIS2

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STUDY NO. : 0222 ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FFMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (O- 2W)

SEX	: FEMALE				PAGE: 8
Organ	Findings	No. of Animals on Study Grade1	6000ppm 1 2 3 4 %) (%) (%)	9000ppm 2 1 2 3 4 (%) (%) (%)	
[Endocrine	system]				
adrena L	hemorrhage	(0) (< 1> 0 0 0 0) (0) (0)	<pre></pre>	
Grade <a>a> b <a>c	1: Slight 2: Moderate a: Number of animals examined at th b: Number of animals with lesion c: a / b * 100	3 : Marked 4 : Severe e site		N	
(HPT150)					BAIS2

APPENDIX A 10-3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY), SACRIFICED ANIMALS (2W)

REPORT TYPE : A1

SEX : MALE

Organ	No	roup Name Control b. of Animals on Study 2 rade 1 2 3 4 (%) (%) (%) (%)	1778ppm 2 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	4000ppm 2 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	ic system]				
bone marrow	congestion	<pre></pre>	(2) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>
	decreased hematopolesis	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
thymus	atrophy	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	karyorrhexis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0)
spleen	karyorrhexis	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>
[Reproductive	e system]				
testis	atrophy	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
epididymis	debris of spermatic elements	<pre></pre>	<pre></pre>	<pre></pre>	<pre></pre>
Grade <a>> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: a/b*100	Marked 4: Severe e	A		
(IIPT150)					DATE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (2W)

REPORT TYPE : A1
SEX : MALE

PAGE: 2 Group Name 6000ppm 9000ppm No. of Animals on Study 2 2 Findings [Hematopoietic system] bone marrow < 2> < 2> congestion 0 0 0 0 0 1 0 0 (0) (0) (0) (0) (0)(50)(0)(0) decreased hematopoiesis 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) thymus < 2> < 2> atrophy 0 0 0 0 0 0 1 0 (0)(0)(0)(0) (0)(0)(50)(0) karyorrhexis 0 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) spleen < 2> < 2> karyorrhexis 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) [Reproductive system] testis < 2> < 2> atrophy 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(50)(0)(0) epididymis < 2> < 2> debris of spermatic elements 0 0 0 0 1 1 0 0 (0)(0)(0)(0) (50) (50) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:a/b*100

(IIPT150)

BAIS2

APPENDIX A 10-4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (2W)

ANIMAL : RAT F344
REPORT TYPE : A1 SEX : FEMALE

Organ	Findings	Group Name Control No. of Animals on Study 2 Grade 1 2 3 4 (%) (%) (%) (%)	1778ppm 2 1 2 3 4 (%) (%) (%) (%)	2667ppm 2 1 2 3 4 (%) (%) (%) (%)	4000ppm 2 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:gland	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Hematopoieti	c system]				
bone marrow	decreased hematopoiesis	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>
thymus	atrophy	<pre></pre>	<pre></pre>	<pre></pre>	<pre></pre>
	karyorrhexis	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0
Digestive sy	stem]				
iver	hemorrhage	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Urinary syst	em]				
cidney	basophilic change	<pre></pre>	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

REPORT TYPE : A1

SACRIFICED ANIMALS (2W)

SEX : FEMALE PAGE: 4 Group Name 6000ppm mag0000 No. of Animals on Study 2 1 3 Findings Organ (%) (%) [Respiratory system] nasal cavit < 2> < 1> 0 0 0 0 respiratory metaplasia:gland 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) [Hematopoietic system] bone marrow < 2> < 1> decreased hematopoiesis 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0) (100) (0) (0) thymus < 2> < 1> atrophy 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(100)(0)(0) karyorrhexis 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(100)(0)(0) [Digestive system] Liver < 2> hemorrhage 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(100)(0)(0) [Urinary system] kidney < 2> < 1> basophilic change 0 0 0 0 . 1 0 0 0 (0)(0)(0)(0) (100) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > b

a: Number of animals examined at the site b: Number of animals with lesion

(c) c : a / b * 100

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1
SEX : FEMALE

4000ppm 2 2 3 4 (%) (%) (%)	_12	<u>4</u> (%)	3	2667) 2 2 (%)	<u>1</u> (%)	<u>4</u> (%)	3 (%)	1778p 2 2 (%)	(b)	1 (%	<u>4</u> (%)	3 (%)	Contr 2 2 (%)		on Study 	up Name of Animals de			indings	·
																				ary syste
<pre></pre>	0	0	0	< 2 0 0) (0 (0) (0 (0)	0 0) (< 2> 0 0) (-	((0) 0 0) (< 2> 1 50) (({	0 (0)		junction	:cortico-medullary	nineralization	у
														re	4: Sever	ı rked	3 : Ma the site	2: Moderate nimals examined at nimals with lesion		
_													·					imals with lesion		

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

Group Name 6000ppm 9000ppm No. of Animals on Study 2 1 2 3 4 2 3 Findings__ (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney · < 1> < 2> mineralization:cortico-medullary junction 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0) (0) (0) (0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:a/b*100(IIPT150) BAIS2

APPENDIX A 10-5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

PAGE: 1

[Digestive system] liver granulation 2 0 0 0 0 0 1 0 0 1 1 0 0 0 1 1 0 0 0 0	4000ppm 2 1 2 3 4 (%) (%) (%) (%)	2667ppm 2 1 2 3 4 (%) (%) (%) (%)	1778ppm 2 1 2 3 4 (%) (%) (%) (%)	Control mals on Study 2 1 2 3 4 (%) (%) (%) (%)	Group Nam No. of An Grade Findings	Organ
Stranulation					system]	(Digestive
basophilic change	2> 1 0 0 0 (50) (0) (0) (0)	1 1 0 0	0 1 0 0	2 0 0 0	granulation	liver
basophilic change 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0					ystem]	Urinary sy
(50) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0 0 0 0 0 (0) (0)	1 0 0 0	0 0 0 0	0 0 0 0	basophilic change	idney
= 1100010	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)		hydronephrasis	
b b: Number of animals with lesion c) c:a/b*100				4 : Severe	a : Number of animals examined at the site b : Number of animals with lesion	a > b

ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : MALE

Group Name 6000ppm 9000ppm No. of Animals on Study 2 2 Grade Findings_ Organ [Digestive system] liver < 2> < 2> granulation 1 1 0 0 0 0 0 0 (50) (50) (0) (0) (0)(0)(0)(0) [Urinary system] kidney < 2> < 2> basophilic change 0 0 0 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) hydronephrosis 0 0 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe < a > a: Number of animals examined at the site b: Number of animals with lesion b (c) c: a / b * 100(IIPT150)

BA1S2

APPENDIX A 10-6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

Organ	Findings	Group Name No. of Animals o Grade	Control on Study 2 1 2 3 4 (%) (%) (%) (%)	1778ppm 2 1 2 3 4 (%) (%) (%)	2667ppm 2 1 2 3 4 (%) (%) (%) (%)	4000ppm 2 1 2 3 4 (%) (%) (%) (%)
(Digestive	e system]					
liver	inflammation		<pre></pre>	<pre></pre>	<pre></pre>	<pre></pre>
	granulation		1 0 0 0 (50) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (50) (0) (0) (0)	1 0 0 0 (50) (0) (0) (0)
Grade <a> b (c)	1 : Slight 2 : Moderate a : Number of animals examined a b : Number of animals with lesion c : a / b * 100		4 : Seuere			
(HPT150)						BAIS

ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : FEMALE

SEX	: FEMALE			PAGE : 4
Organ	Findings	Group Name 6000ppm No. of Animals on Study 2 Grade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	
[Digestive	e system]			
liver	inflammation	<pre></pre>	<pre></pre>	
	granulation	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (50) (0) (0)	
Grade (a) b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: a/b*100	3: Marked 4: Severe site		
(HPT150)				BAIS2

APPENDIX A 11-1

IDENTITY OF GLYOXAL

(TWO-WEEK STUDIES)

IDENTITY OF GLYOXAL (TWO-WEEK STUDIES)

Test Substance Lot No.: WDL5585

1. Spectral data

Mass Spectrometry

Instrument:

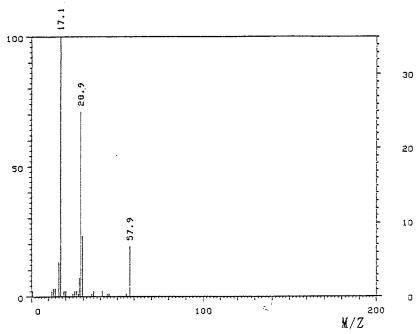
Hitachi M-80B Mass Spectrometer

Ionization:

El(Electron Ionization)

Ionization Voltage:

70eV



Mass Spectrum of Test Substance

Results:	<u>Determined</u>	<u>Literature Value*</u>		
	Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)		
	57. 9	58-0		
	28.9	29.0		
	17. 1	17.0		
		(*EPA/NIH Mass Spectral Data Base (1978) V. 1,		

p. 7.)

2. Conclusions: The result of the mass spectrum agreed with the literature value. Consequently, the test substance was identified as glyoxal.

APPENDIX A 11-2
STABILITY OF GLYOXAL
(TWO-WEEK STUDIES)

STABILITY OF GLYOXAL(TWO-WEEK STUDIES)

Test Substance Lot No.: WDL5585

1. Sample storage: This lot was used from 1992.10.26 to 1992.11.16. Test substance

was stored at room temperature.

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gass Chromatograph

Column:

Methyl Silicone(0.2mm $\phi \times 50$ m)

Column Temperature:

200°C

Flow Rate:

1 ml/min

Detector:

FID(Flame Ionization Detector)

Injection Volume:

 $1 \mu 1$

Pre-Treatment:

Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution (1ml). This mixture was stirred at 75° C for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and

analyzed.

Results:

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Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992.10.9 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992.11.17. The new treace impurity peak in

the test substance analyzed at 1992.11.17 was not

detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1992.10.9 (date analyzed)	1 2	2.838(Solvent peak) 3.473	1.00	100
1992.11.17 (date analyzed)	1 2	2.837(Solvent peak) 3.47	1.00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 6 weeks).

APPENDIX A 11-3 CONCENTRATION GLYOXAL IN DRINKING WATER (TWO-WEEK STUDIES)

CONCENTRATION OF GLYOXAL IN DRINKING WATER (TWO-WEEK STUDIES)

(Rat)(Mouse)

		Target Concentration(ppm)						
Date analyzed	1778	2667	4000	6000	9000			
1992. 10. 26	1702.9(95.8)*	2644.7(99.2)	3972.5(99.3)	5893.9(98.2)	8940.6(99.3)			

(*) % of target concentration

Analytical method: The sample were analyzed by the gas chromatography.

Instrument

: Hewlett Packard 5890A

Flow Rate

: lml/min

Column

Carrier

: METHYL SILICONE(0.2mm $\phi \times 50$ m)

Detector

: FID(Flame Ionization Detector)

Column Temperature: 200°C

Injection Volume

 $: 1 \mu 1$

Pre-Treatment

: He

: Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75°C for 0.5 hr. Then, this

solution was extracted with ethyl acetate(2ml) and analyzed.

APPENDIX A 11-4 STABILITY OF GLYOXAL IN DRINKING WATER (TWO-WEEK STUDIES)

STABILITY OF GLYOXAL IN DRINKING WATER (TWO-WEEK STUDIES)

(Rat)

	Target Concenti	ration(ppm)
Date analyzed	1778	9000
1992.10.09(a)	1825	9148
1992.10.16(b)	1799	8730
OUSE)		
	Target Concentr	ration(ppm)
Date analyzed	1778	9000
1992.10.09(a)	1825	9148
1992.10.16(b)	1872	

⁽a) Date of preparation

Analytical method: The sample were analyzed by the gas chromatography.

Instrument : lle

: Hewlett Packard 5890A

Flow Rate

: lml/min

Column

Carrier

: METHYL SILICONE(0.2mm $\phi \times 50$ m)

Detector

: FID(Flame Ionization Detector)

Column Temperature: 200°C

e: 200°C : lle Injection Volume

 $: 1 \mu 1$

Pre-Treatment

: Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75°C for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

⁽b) The stability of glyoxal in drinking water was established for 7 days when stored at $25 \, ^{\circ}\!\! \mathrm{C}$.